Lecture 10

Maximum likelihood

Botany 563 — Spring 2022

- **Previous class check-up:**
    - We studied the different models of evolution
- **Learning Objectives:** At the end of today's session, you will be able to
    - Explain how the likelihood of a tree is computed
    - Explain the steps in maximum likelihood phylogenetic inference
- **Pre-class work**
    - Read HAL 1.2 and canvas quiz

Phylogenetic inference

Step 1: Choose the criterion to use: distances, parsimony, likelihood

Step 2: Search the space of trees until you find the optimum

Phylogenetic inference

Step 1: Choose the criterion to use:
~~distances, parsimony~~, likelihood

Step 2: Search the space of trees
until you find the optimum

You know how to calculate the likelihood for a given tree

Maximum likelihood

1. Choose a substitution model

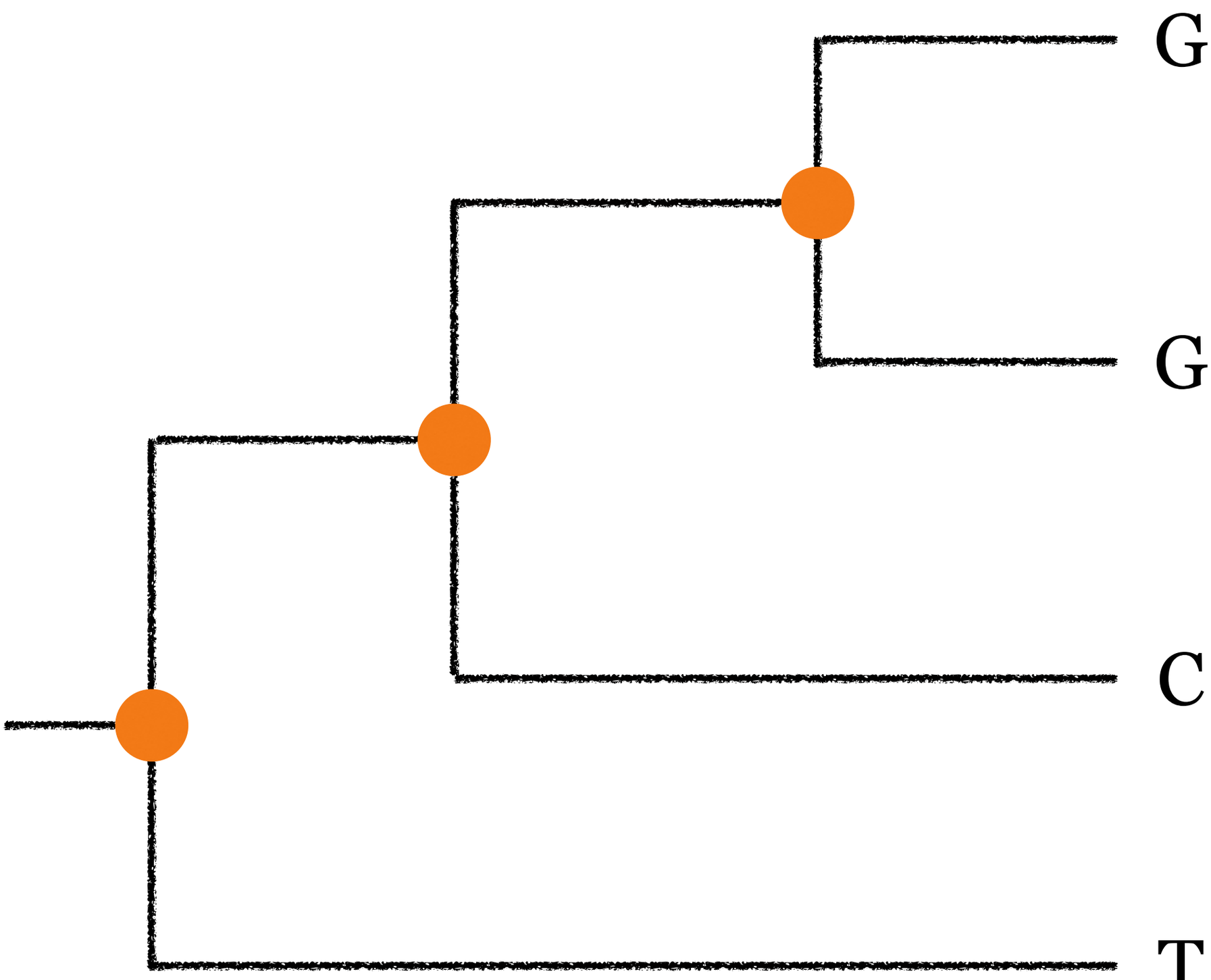
$$\mathbf{P}(t) = \begin{array}{c|cccc} & A & C & G & T \\ \hline A & & & & \\ C & & & & \\ G & & & & \\ T & & & & \end{array} = e^{\mathbf{Q}\mu t}$$

2. For a given tree, calculate the likelihood given the data and the substitution model

$$\mathcal{L}_{\mathbf{Q}}\left(\begin{array}{l} \text{AAGTCTAG} \\ \text{AAGTCTAG} \\ \text{AACTCTAG} \\ \text{AATTCTAG} \end{array} \right)$$

3. Search the space of trees using the tree moves (NNI, SPR, TBR) until you find the maximum likelihood tree

Calculate the likelihood for this tree

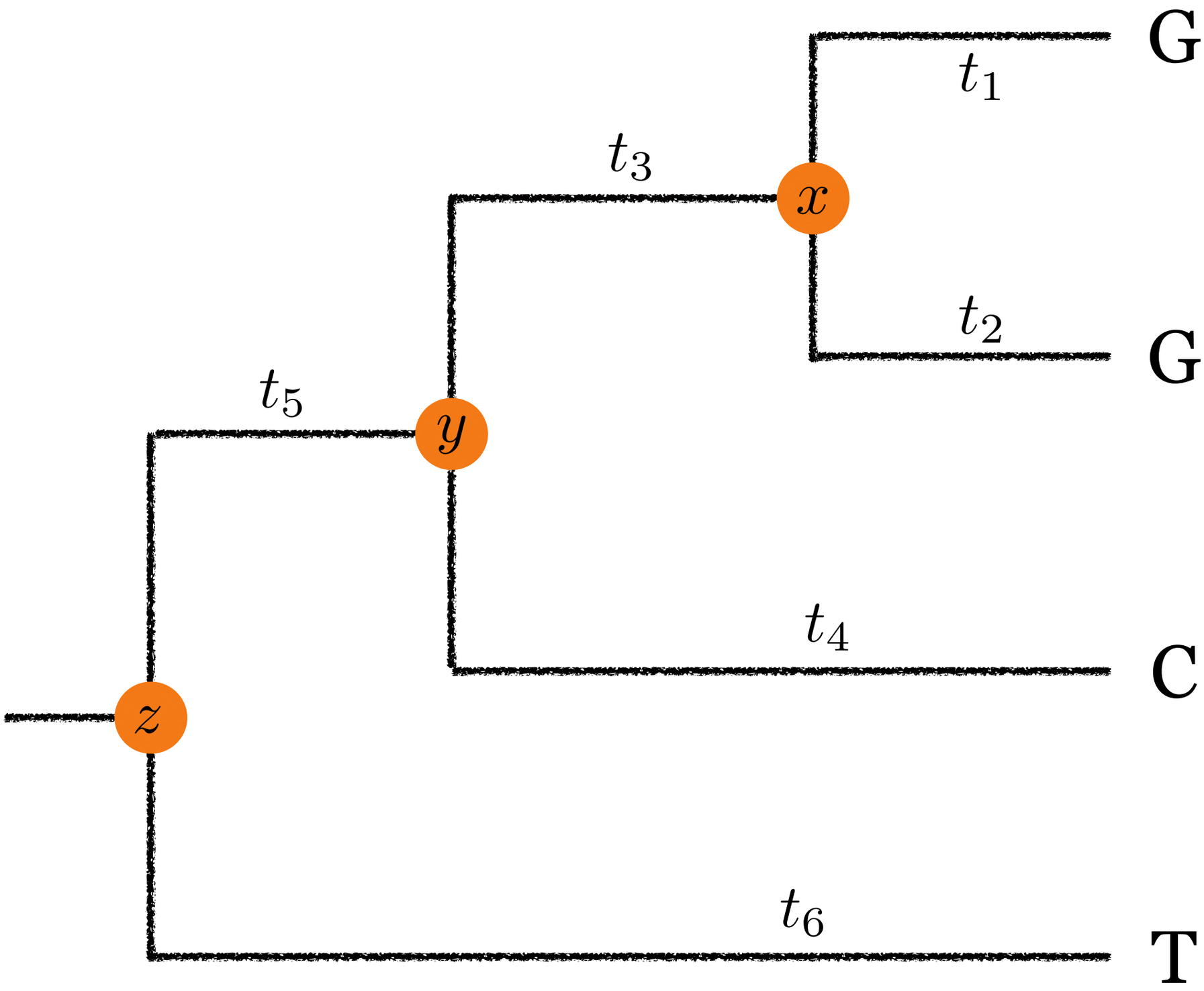


Assumption 1: The mutation process is the same at every branch of the tree

Assumption 2: We assume sites evolve independently

Assumption 3: All sites evolve the same

Calculate the likelihood for this tree



Depends on parameters:

$\mathbf{Q}$ You choose which form (each model has its own parameters)

$\mathbf{t} = (t_1, \ldots, t_6)$ Branch lengths

x, y, z Ancestral states

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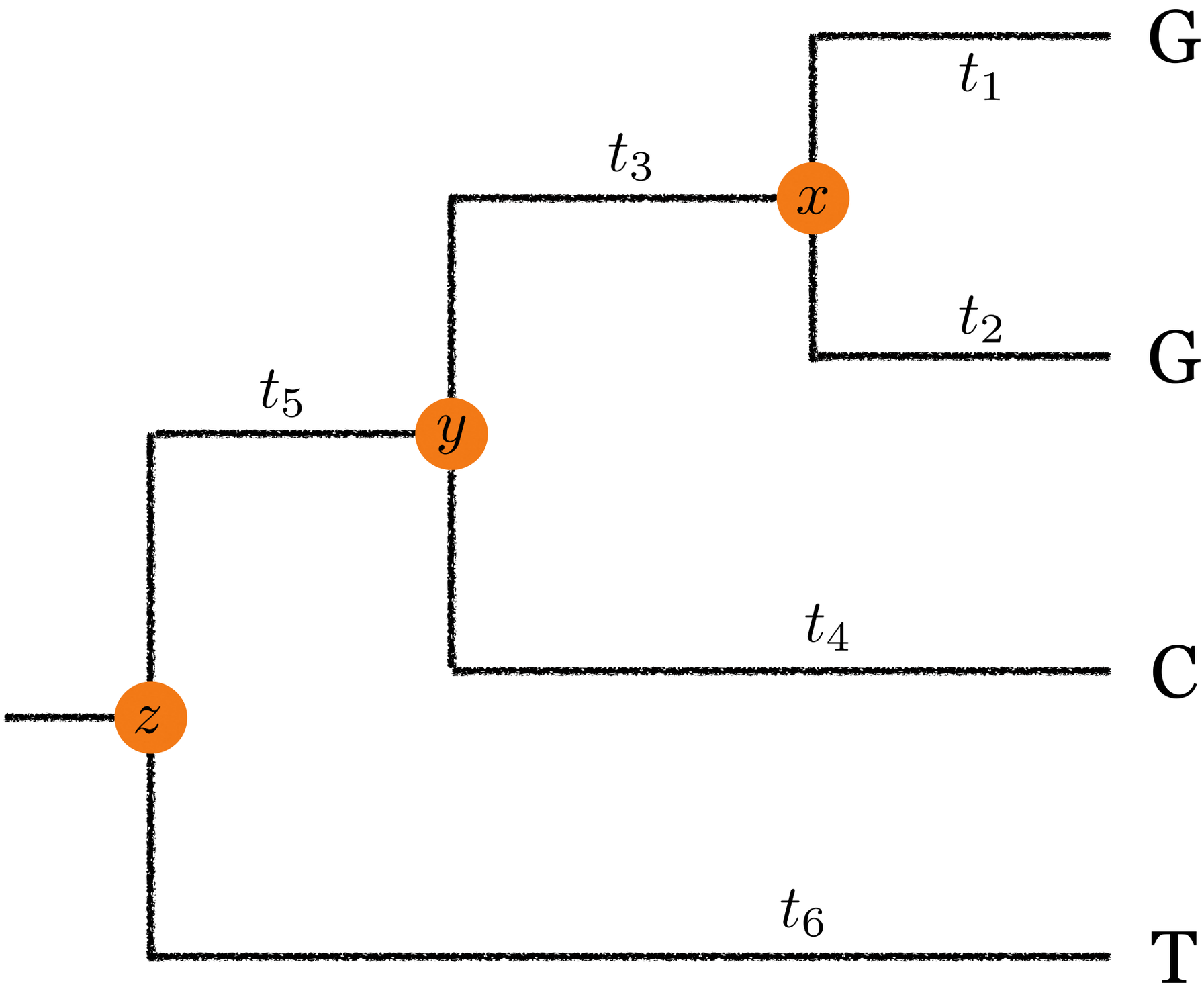

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$$\mathcal{L}(T, \mathbf{Q}, \mathbf{t}, x, y, z)$$

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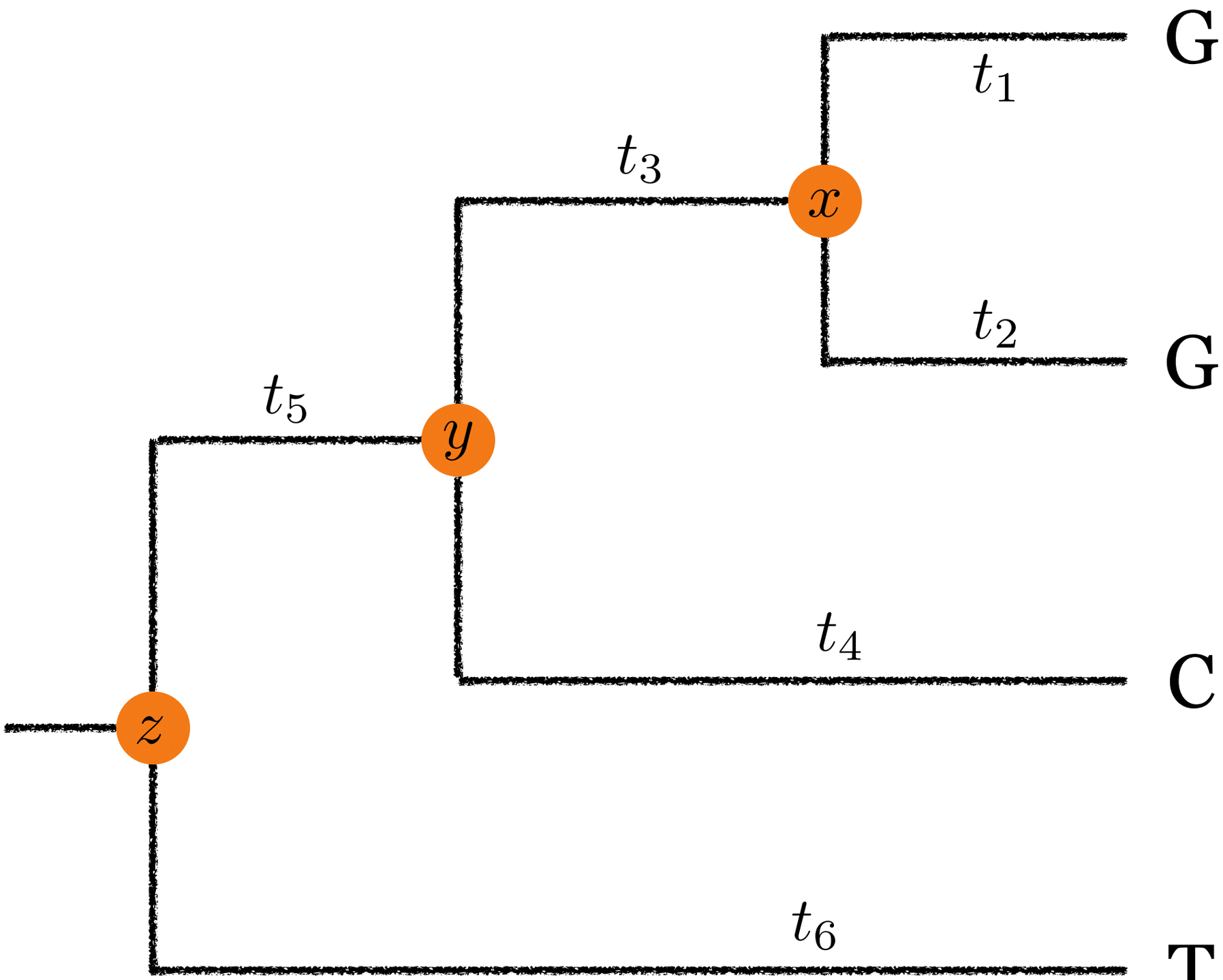

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$$\mathcal{L}(T, \mathbf{Q}, \mathbf{t}, x, y, z) = P(GGCT|T, \mathbf{Q}, \mathbf{t}, x, y, z)$$

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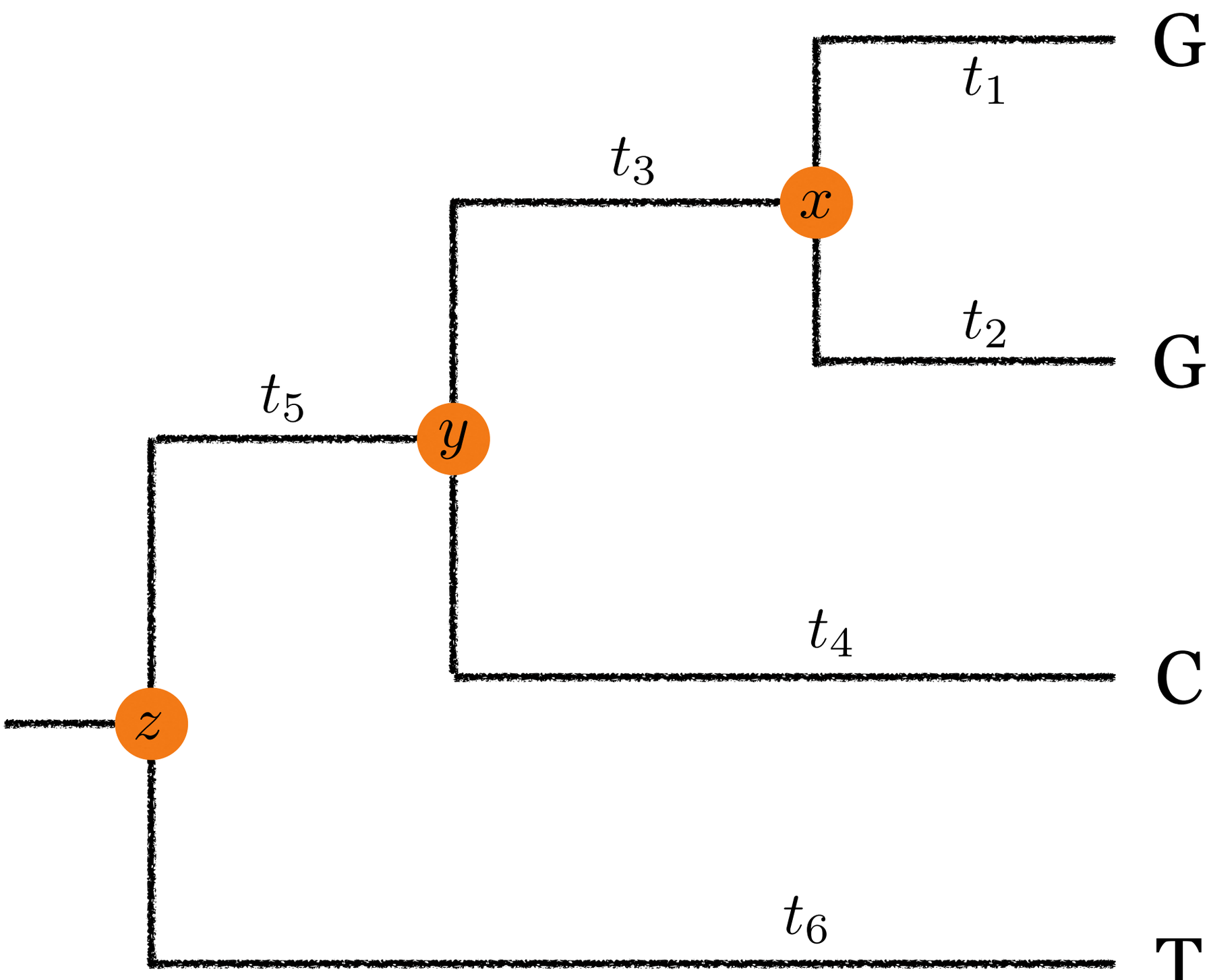

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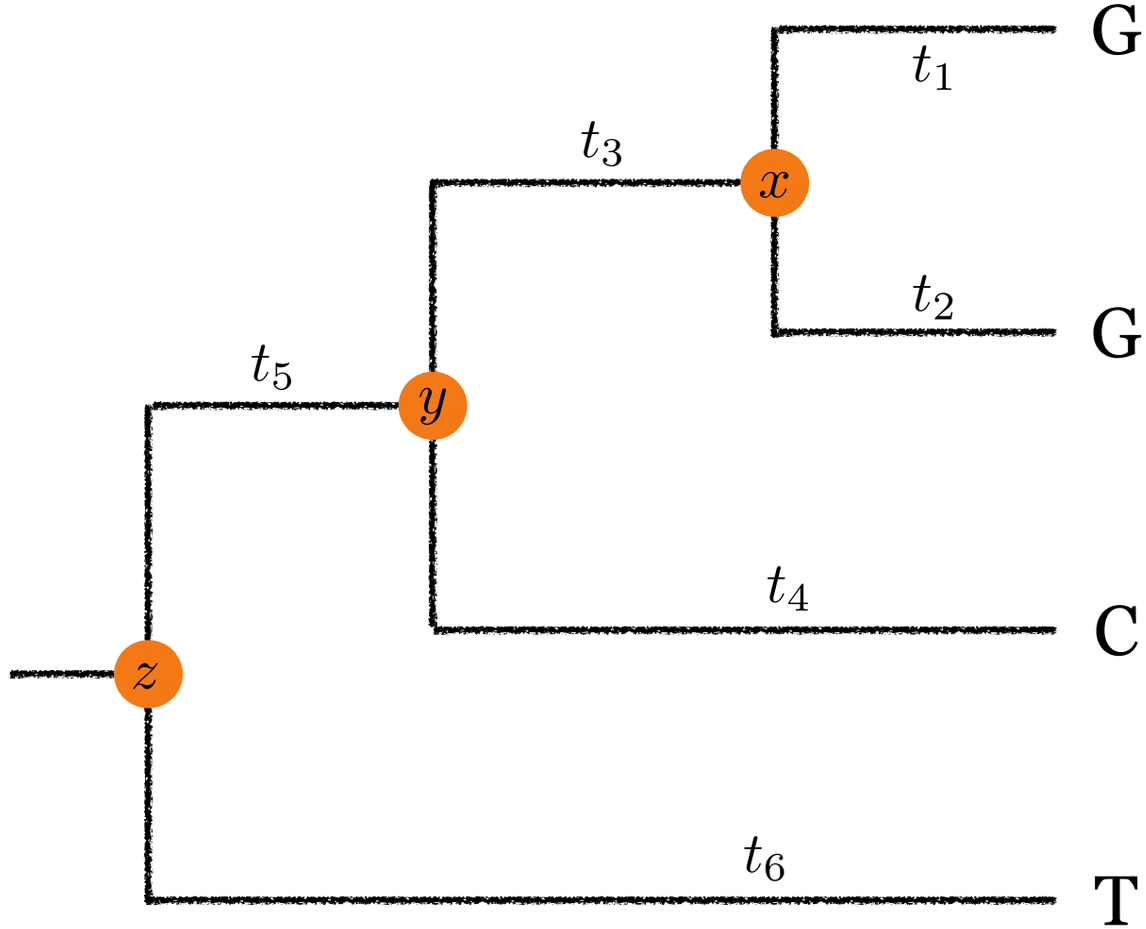

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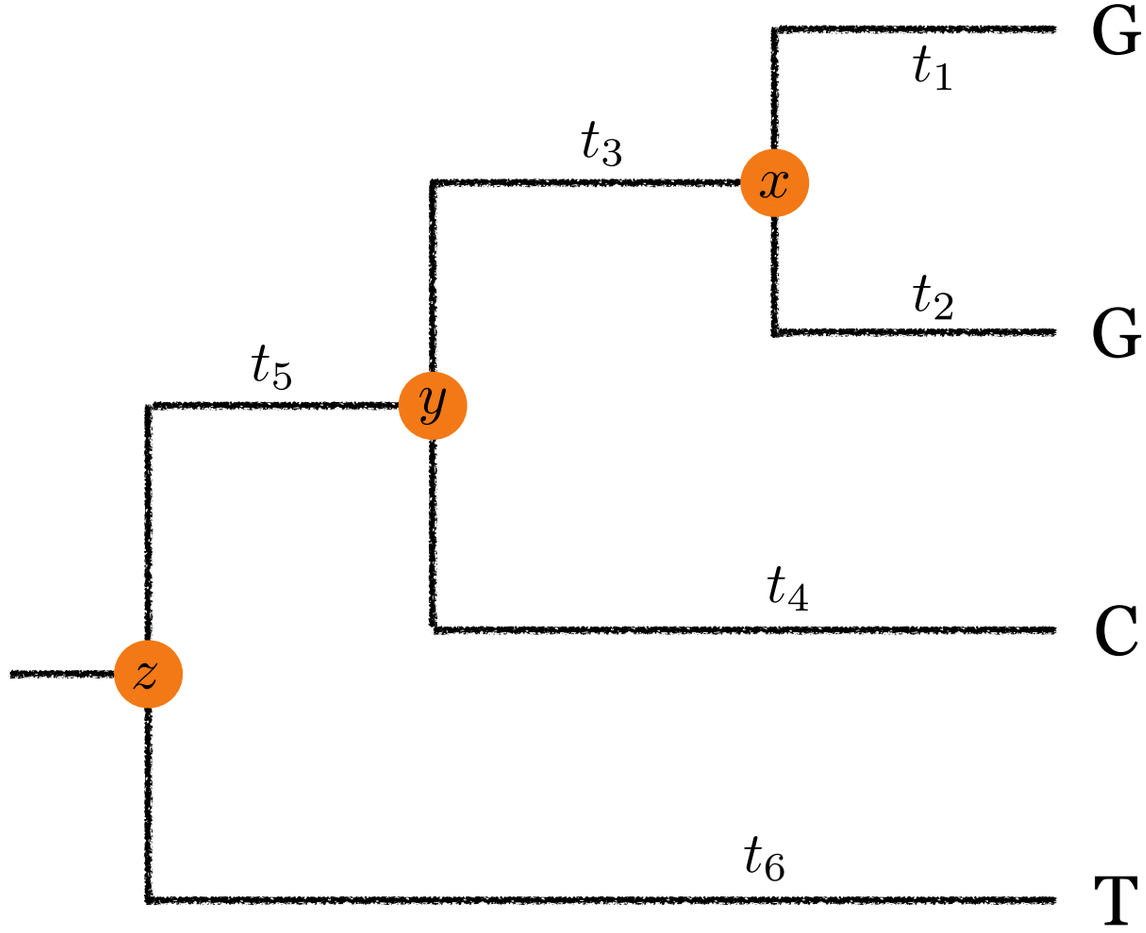
Calculate the likelihood for this tree

$$\mathbf{P}(t) = e^{\mathbf{Q}\mu t}$$

$$\mathbf{Q} = \begin{array}{c} \begin{matrix} A & C & G & T \end{matrix} \\ \begin{bmatrix} * & a\pi_C & b\pi_G & c\pi_T \\ a\pi_A & * & d\pi_G & e\pi_T \\ b\pi_A & d\pi_C & * & f\pi_T \\ c\pi_A & e\pi_C & f\pi_G & * \end{bmatrix} \end{array} \begin{matrix} A \\ C \\ G \\ T \end{matrix}$$



$$L = \sum_z \sum_y \sum_x \pi(z) P_{t_6}(z, T) P_{t_5}(z, y) P_{t_4}(y, C) P_{t_3}(y, x) P_{t_2}(x, G) P_{t_1}(x, G)$$

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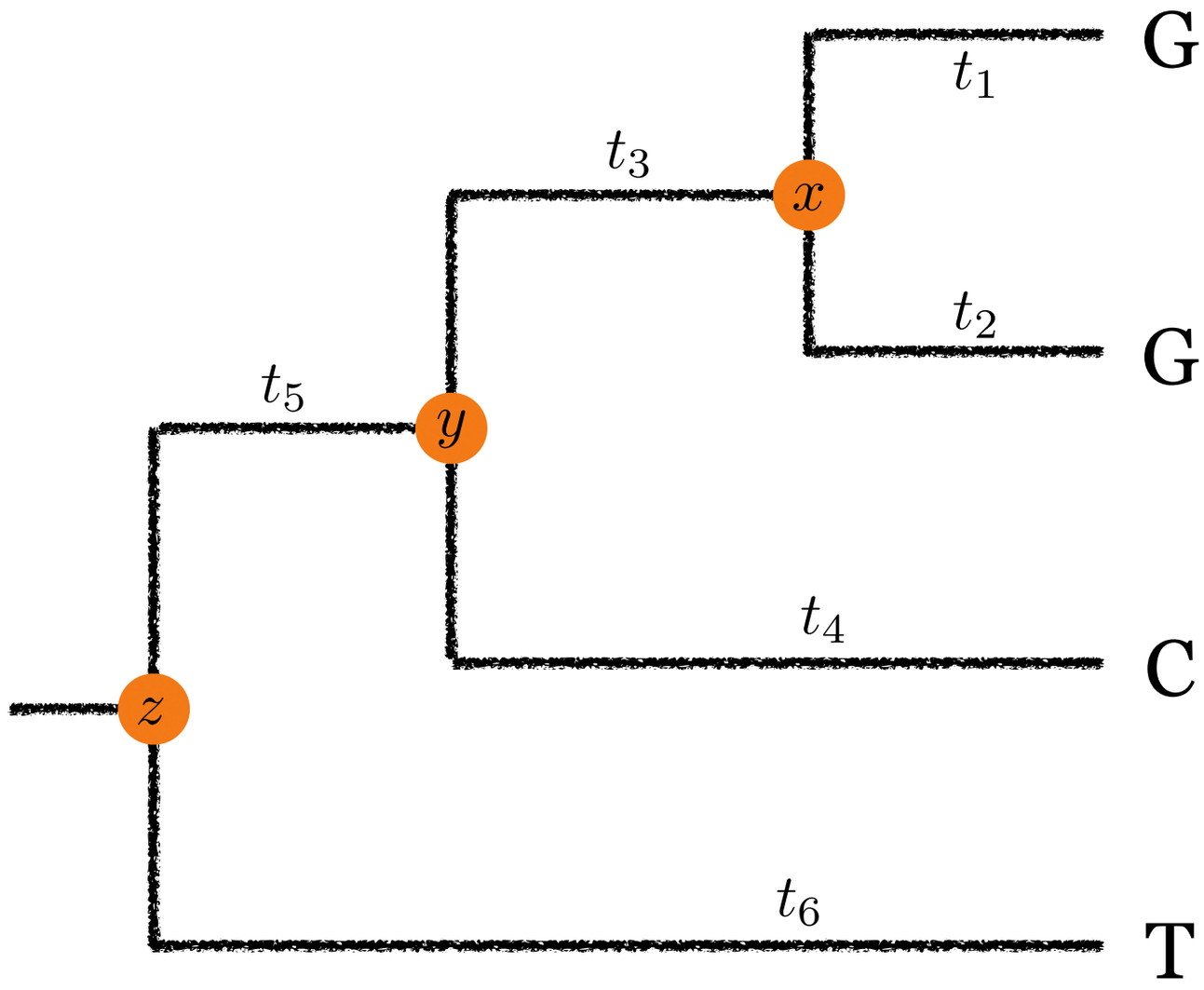

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Where do the assumptions play a role?

Assumption 1: The mutation process is the same at every branch of the tree

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Felsenstein's pruning algoritm

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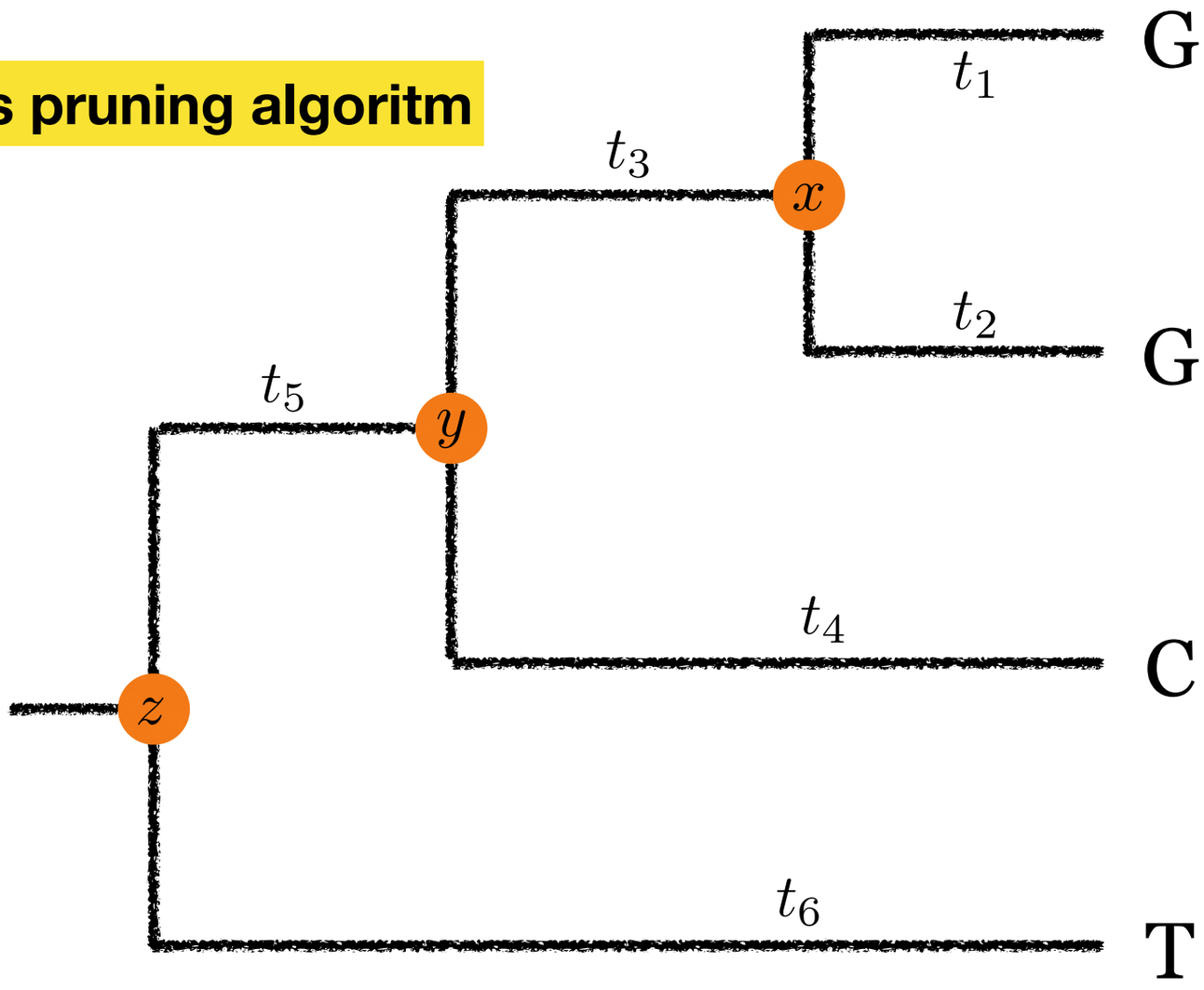

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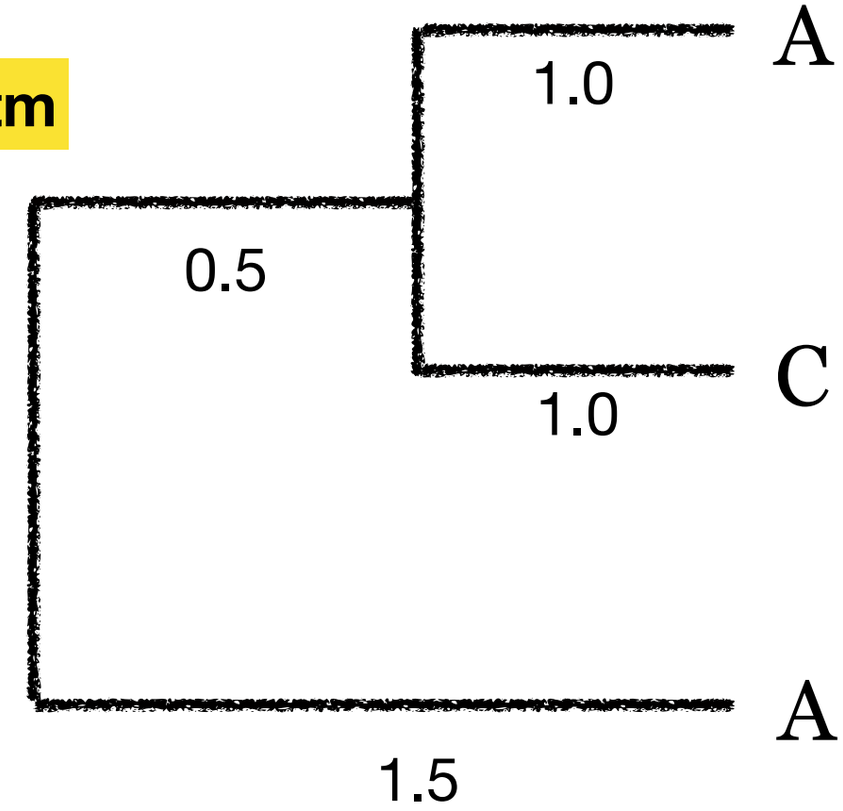

$$L_p(i) = \left(\sum_x P(x|i, t_L) L_L(x) \right) \left(\sum_x P(x|i, t_R) L_R(x) \right)$$

Full example in video on YouTube

Maximum likelihood

1. Choose a substitution model

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Need to optimize

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➡ At each proposed tree, we maximize Q and t

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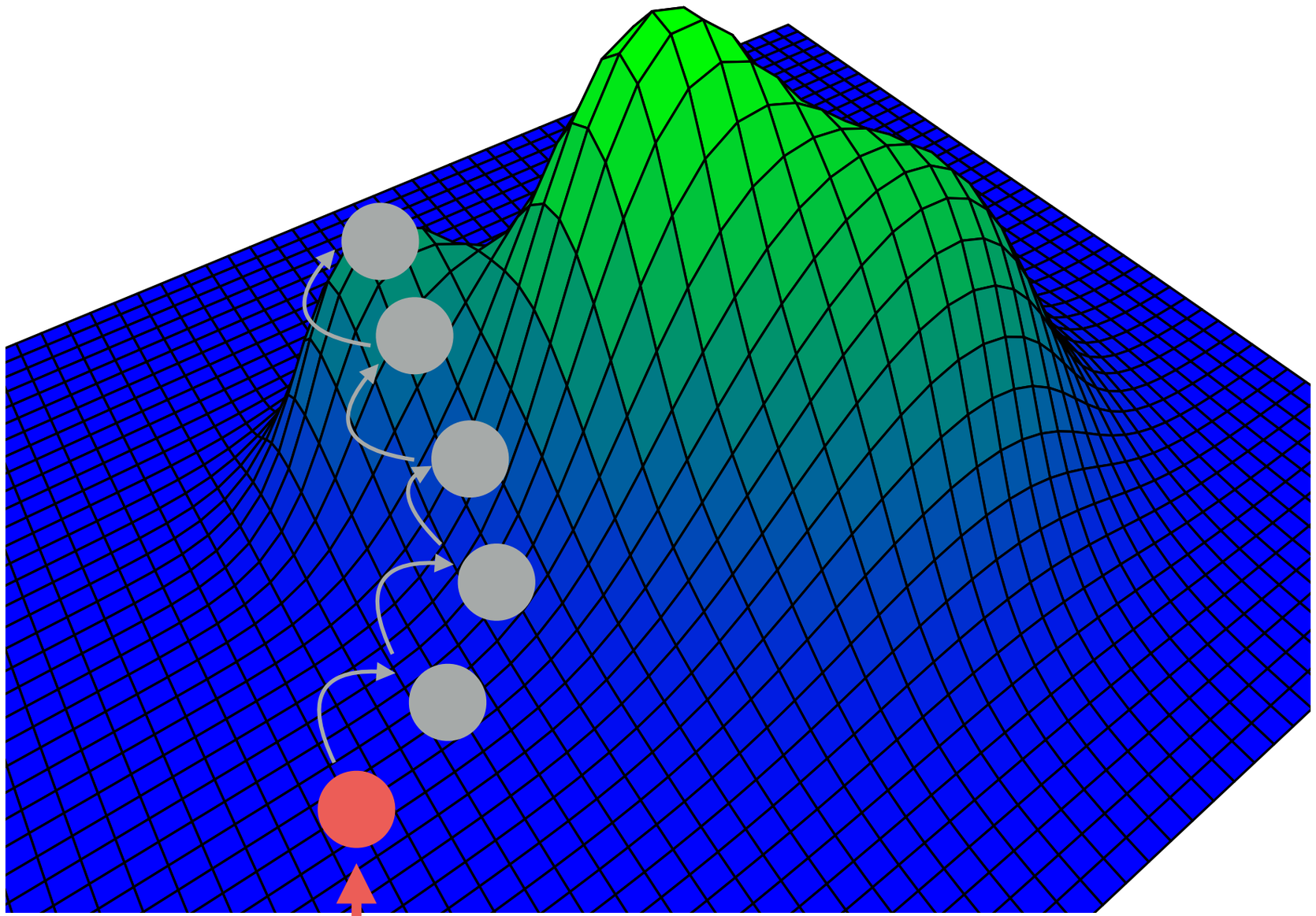
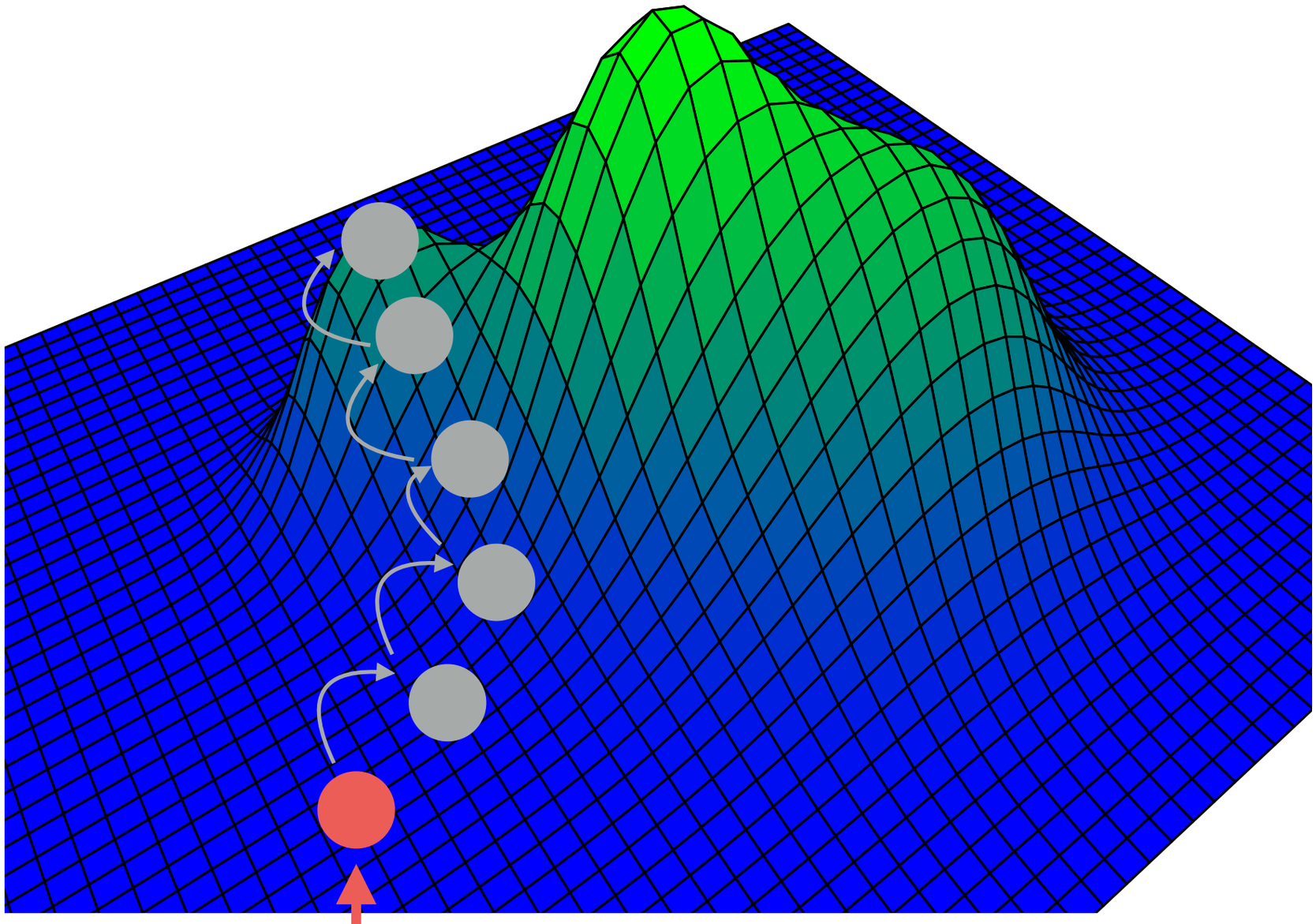
Traverse tree space: finding the MLE



Starting tree

Nearest Neighbor Interchange (NNI)
Subtree Pruning and Regrafting (SPR)
Tree Bisection and Reconnection (TBR)

Traverse tree space: finding the MLE

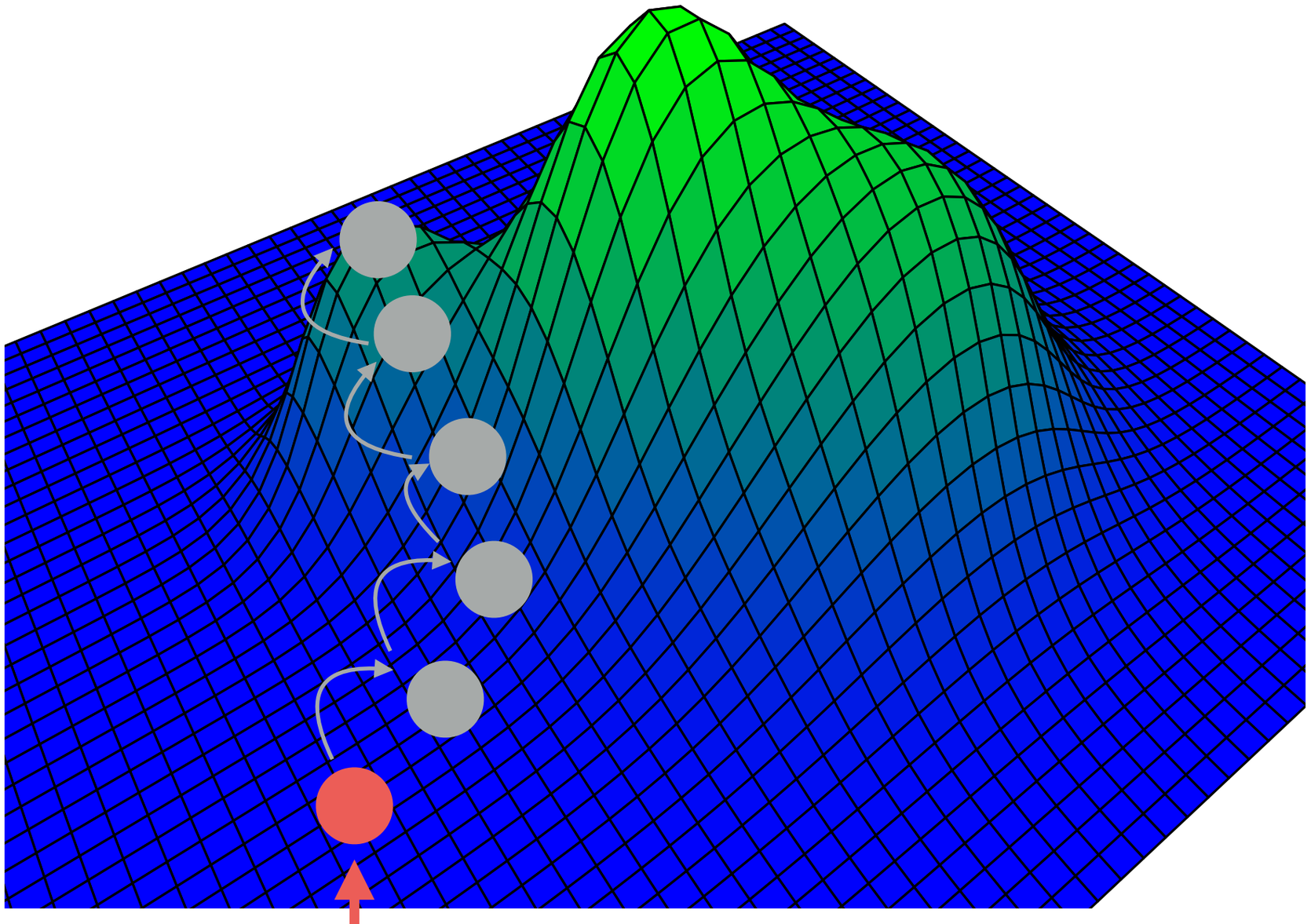


Starting tree

Four things affecting performance:

- Starting tree
- Model chosen
- Data
- Convergence

Traverse tree space: finding the MLE



Starting tree

Four things affecting performance:

- Starting tree
  - Affects optimization
  - Get stuck on poor likelihood region
  - Bad starting tree?
    - Best case: slows down
    - Worst case: suboptimal tree
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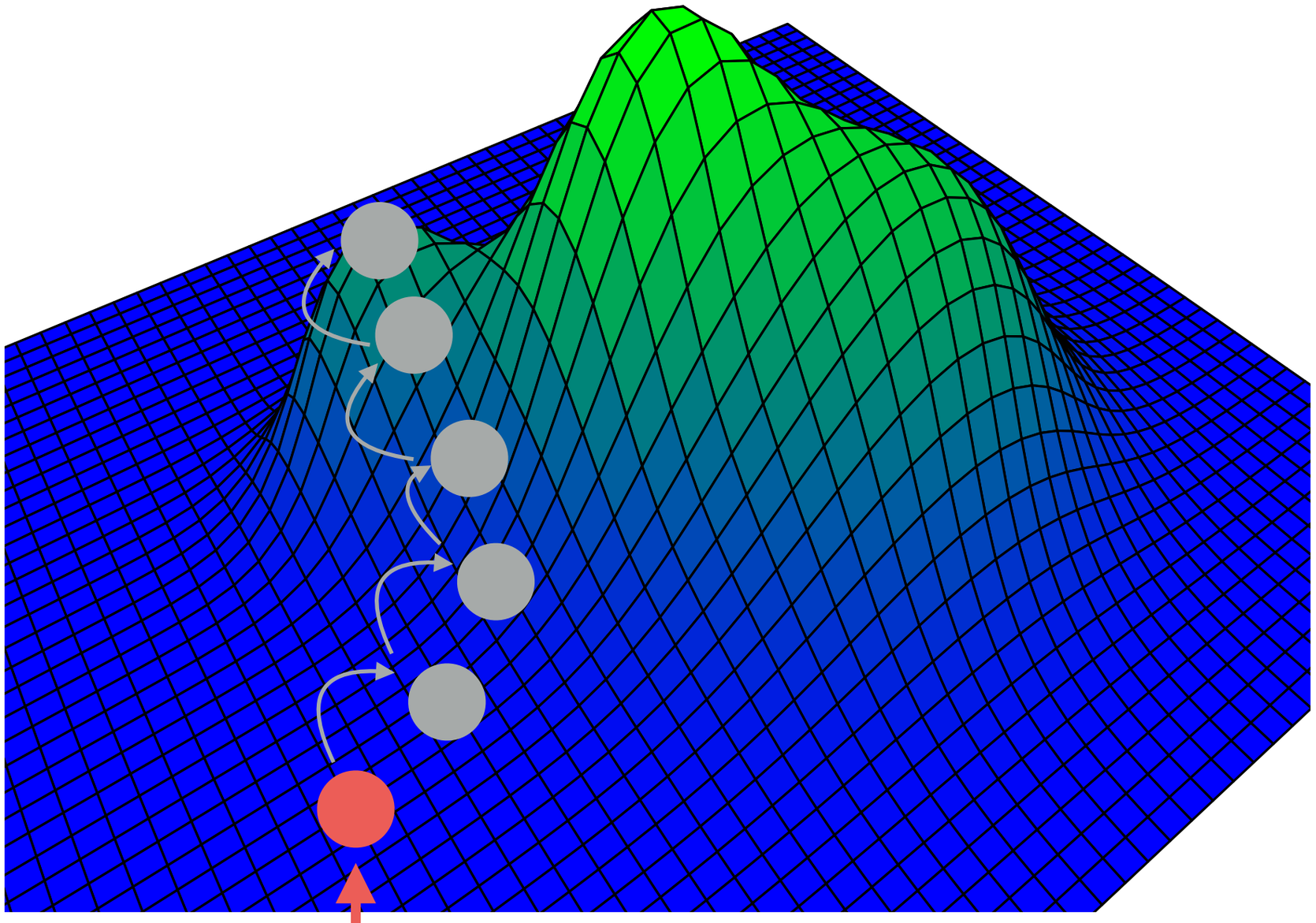
Traverse tree space: finding the MLE



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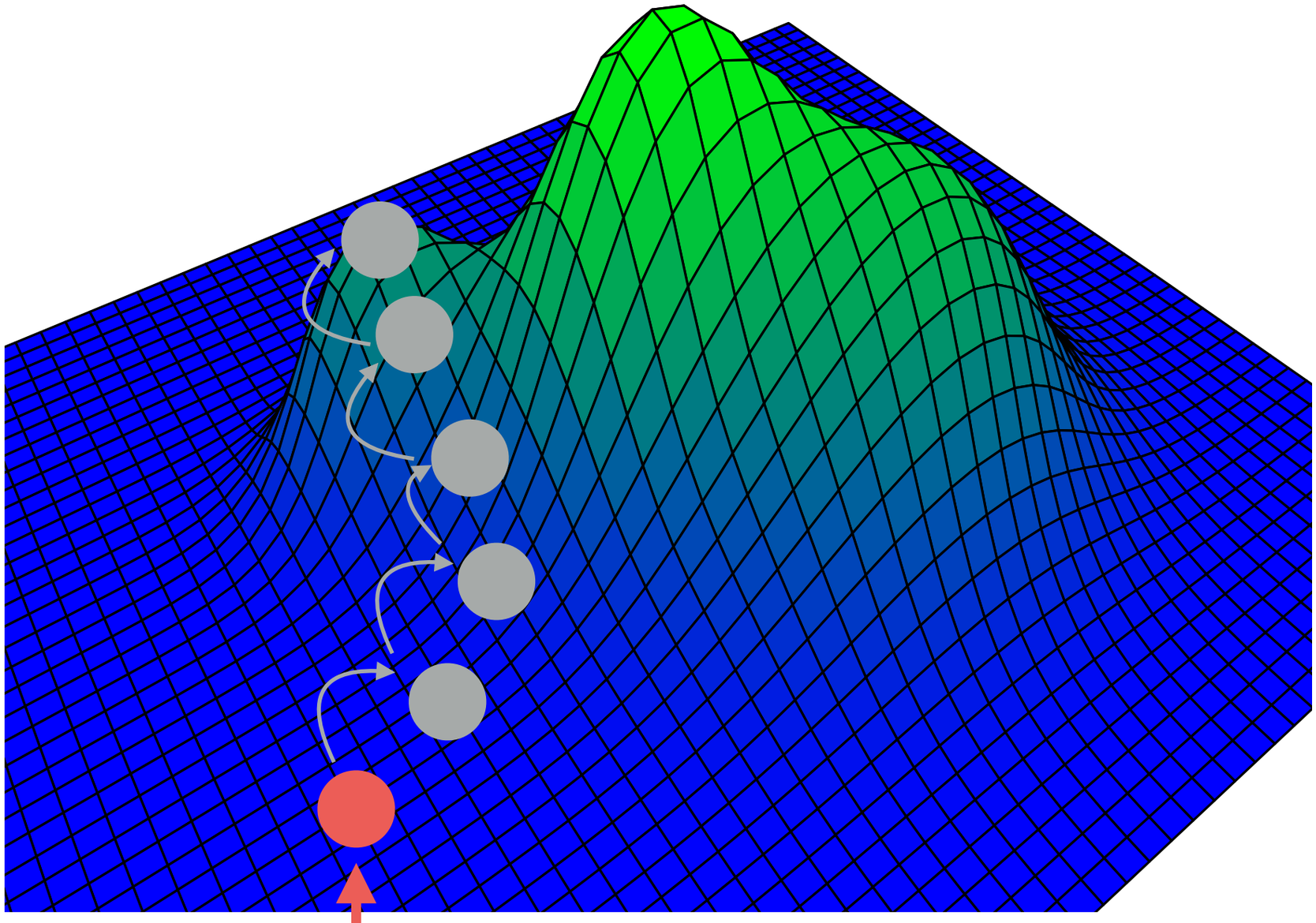
  - Affects shape of the surface we optimize
  - You might be optimizing the wrong function
  - Identifiability
- Data
- Convergence

Traverse tree space: finding the MLE



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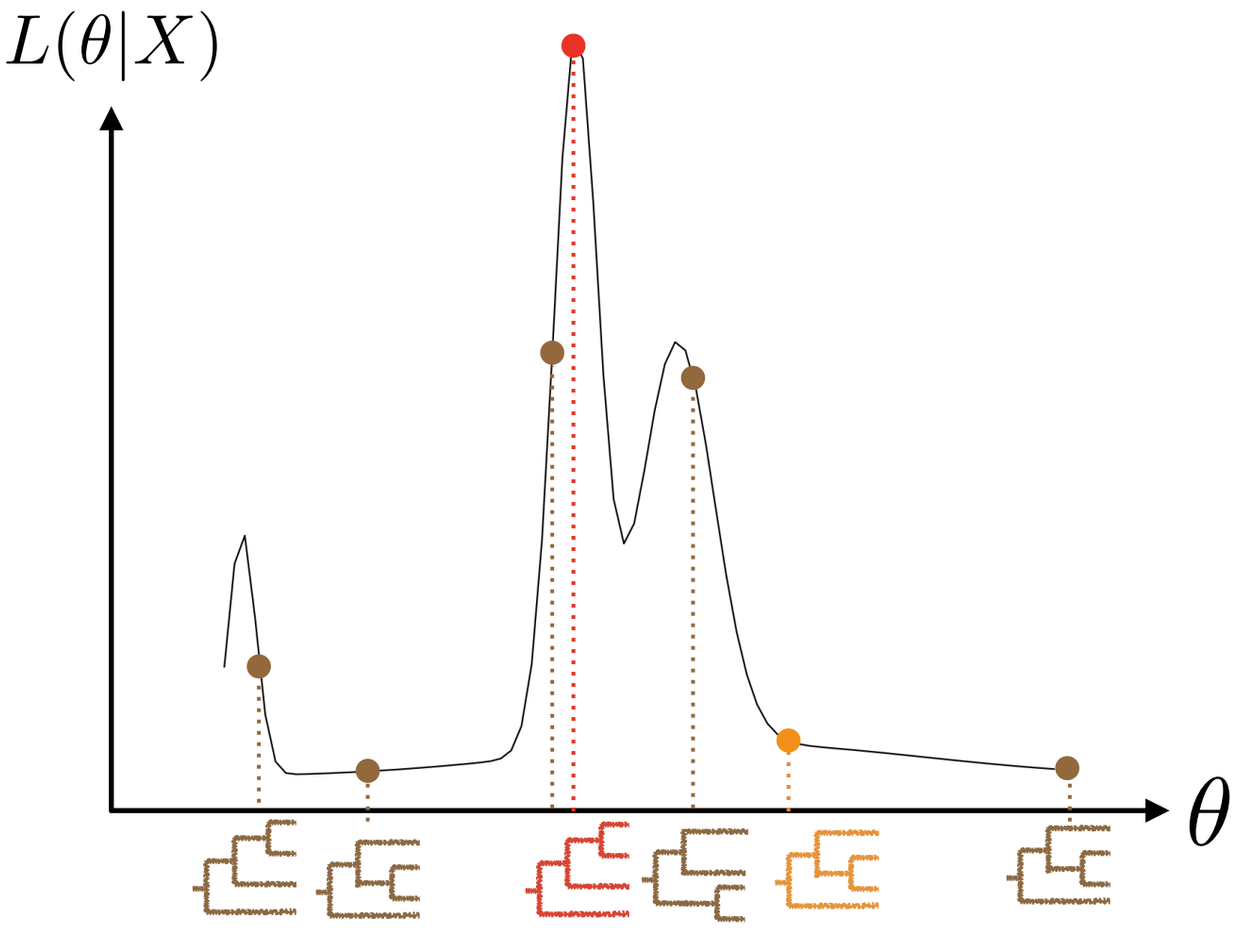
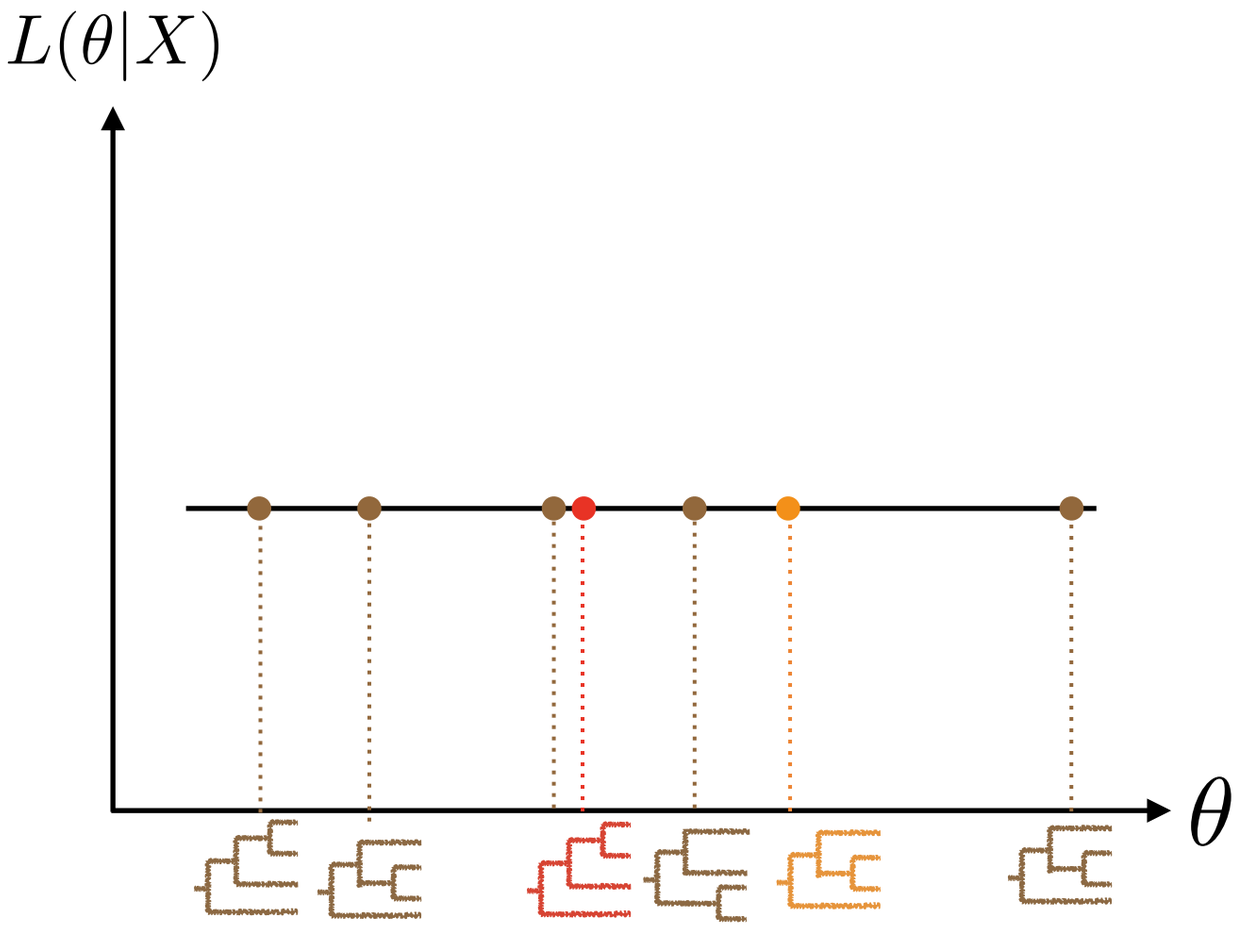
HAL 1.2 "Rough likelihood surface: when analyzing datasets with comparatively few sites and a large number of taxa. The key challenge with such datasets is that 100 distinct ML searches are likely to yield 100 topologically substantially different, but statistically indistinguishable trees."

Identifiability





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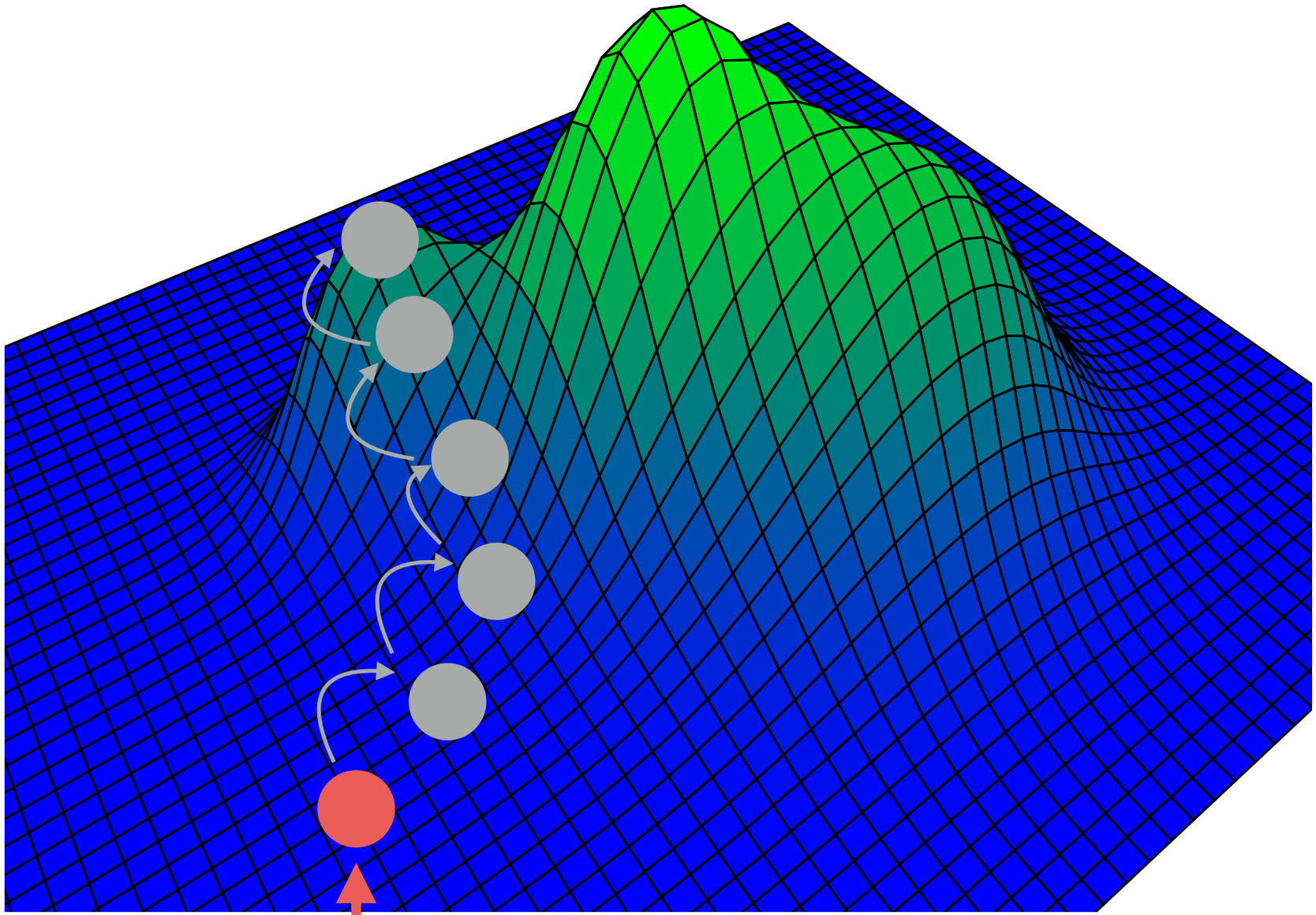

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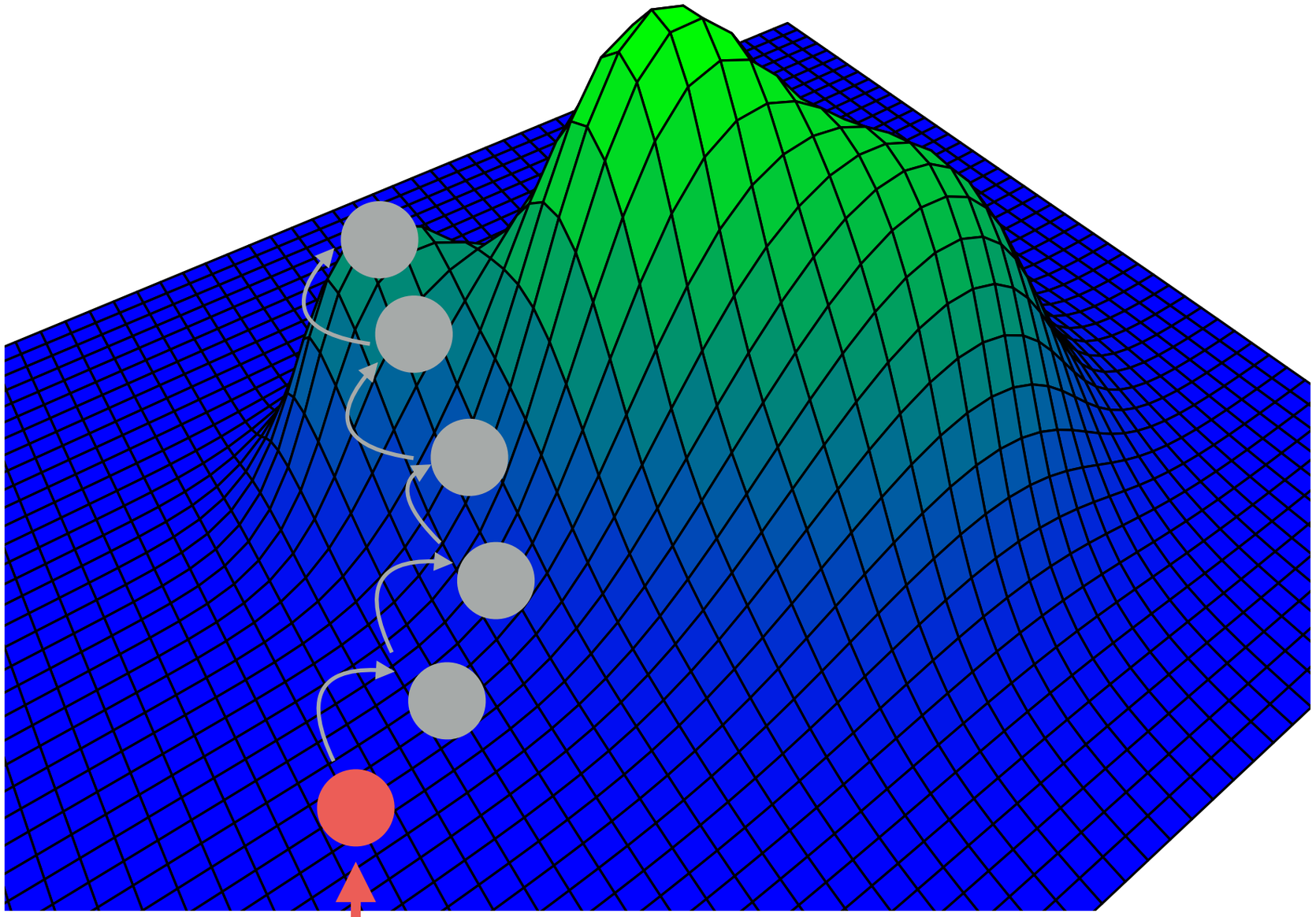
- Data
  - Lack of signal (sample size or poorly chosen region)
  - Difference between data and information
  - Identifiability
- Convergence

Traverse tree space: finding the MLE



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  - When do you stop the traversal of tree space?
  - Affects optimization

Statistical Consistency

- Maximum likelihood (and Bayesian), neighbor joining, ME OLS are all statistically consistent methods

- UPGMA and maximum parsimony are not statistically consistent methods

For next class:

- We will go over IQ-Tree and RAxML
- Each student is assigned to one software and has to read two papers for that software (software papers are short: two papers are fewer than 9 pages combined)
- Focus on the 4 things affecting performance: starting tree, model chosen, data, convergence
- We will have a class discussion followed by installing and using the software